EP00 03517

The Patent Office

INVESTOR IN PEOPLE

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed Andrew George

Dated 27 JAN 2000

Patents Form 1/77

Act 1[illegible]
([illegible])

The Patent Office

[illegible] R99 E442234-3 D10009 [illegible]
[illegible] 0.00 - 9909358.5

RECEIVED BY POST
24 APR 1999
THE PATENT OFFICE

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference CGP/PG3681

2. Patent application number
(The Patent Office will fill in this part) 9909358.5 24 APR 1999

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

GLAXO GROUP LTD
GLAXO WELLCOME HOUSE
BERKELEY AVENUE
GREENFORD
MIDDLESEX UB6 ONN
UNITED KINGDOM

Patents ADP number *(if you know it)* 4735870002

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention

PACKAGING METHOD

5. Name of your agent *(if you have one)*

DR CHRISTOPHER G PIKE
PIKE & CO.
3 KLONDYKE
MARLOW
BUCKS
SL7 2DQ

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Patents ADP number *(if you know it)* 7497936001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

YES

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	0
Description	8
Claim(s)	3
Abstract	1
Drawing(s)	4

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature [signature] Date 23 APRIL 99

DR CG PIKE - AGENT FOR THE APPLICANT

12. Name and daytime telephone number of person to contact in the United Kingdom

DR C G PIKE 01628 471869

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) *If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.*

b) *Write your answers in capital letters using black ink or you may type them.*

c) *If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.*

d) *If you have answered 'Yes' Patents Form 7/77 will need to be filed.*

e) *Once you have filled in the form you must remember to sign and date it.*

f) *For details of the fee and ways to pay please contact the Patent Office.*

Packaging method

This invention relates to a method of forming a blister pack involving the use of laser welding techniques. The blister pack is particularly suitable for the containment of medicament in dry powder form.

The use of blister packs as packaging for medicament is well known. Such packs are typically formed by taking a base sheet having a blister pocket therein and affixing a cover sheet thereto to form a seal to the blister pocket. Known methods of fixing the cover sheet to the base sheet include the use of adhesives and welding methods selected from hot metal welding, radio frequency welding and ultrasonic welding.

The use of adhesive sealing can involve problems with controlling the spread of adhesive to ensure even adhesion of the cover sheet to the base sheet and to prevent wastage and mess.

The use of currently known welding methods has the disadvantage that controlled physical contact is required between the welding head and the substrate to be welded. This places a limitation on the speed of the welding process, which is itself required to be mechanically complex. Furthermore, with known welding methods it is difficult to produce complex weld patterns such as zig-zags and dot patterns.

The applicants have now found that the disadvantages of the above-described sealing methods can be overcome if laser welding is employed as the method of sealing the blister pack. In particular, the use of laser welding reduces process complexity overall but allows for the creation of complex weld patterns. Whilst laser welding is a known technique, the advantages of its use in the formation of blister packs has not hitherto been recognised.

Further advantages of the use of laser welding in the fabrication of the blister packs of the invention include precisely controllable low weld energy enabling the weld to be formed in a precise manner without affecting any of the other parts of the blister pack. Laser welds are furthermore clean and may be engineered to be hermetic in nature to achieve good moisture protection properties. Also, since laser output is typically very stable it is possible to achieve consistent weld repeatability.

Still further advantages are achievable when the blister packs are formed from base and/or cover sheets comprising laminates of different materials. The energy of the laser source may be chosen to weld only selective parts of the laminate together whilst maintaining the integrity of the other parts of the laminate. For example, the laser energy source may be tuned to pass through plastic layers in a laminate but to have a welding effect on any adjacent metal layers.

PCT Patent application no. WO98/16430 describes a method and apparatus for laser welding of plastic materials to form plastic bags. No mention is made of blister packs for use in the containment of medicament.

According to one aspect of the present invention there is provided a method of forming a blister pack comprising contacting a base sheet having a blister pocket therein with a cover sheet and applying laser energy to form a seal between said cover sheet and said blister pocket of said base sheet.

Suitably, the base sheet has a plurality of blister pockets therein and laser energy is applied to form a seal between the cover sheet and each blister pocket of said base sheet. Preferably, the base sheet and cover sheet are elongate (e.g. elongate strips) and the base sheet has a plurality of blister pockets spaced therealong. More preferably, laser energy is applied to seal each blister pocket of the elongate base sheet in a sequential fashion.

Suitably, the method comprises pre-filling the or each blister pocket with medicament. Any known filling method is suitable. A suitable filling method involves directly plunging the open blister pocket into a reservoir of powder, thereby causing powder to be forced into the pocket. Another suitable filling method involves the use of hollow transfer pins. The pins are plunged into a powder reservoir such that powder is retained therein, the pins then brought into registration with the pockets to be filled and the powder forced therefrom (e.g. by use of a piston ejection system) into the pockets.

Preferably, the medicament is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof. More preferably, the medicament is in dry powder form.

In one aspect, the laser energy derives from a laser source which is movable relative to the base and cover sheet to enable correct positioning of the seal.

In another aspect, the laser energy derives from a fixed laser source and the base and cover sheet are movable to enable correct positioning of the seal.

In a further aspect, the laser energy is guidable by means of a guide mechanism to enable correct positioning of the seal. Preferably, the guide mechanism includes one or more movable mirrors.

Preferably, the seal is a hermetic seal.

In one aspect, the seal has a zig-zag configuration. In another aspect, the seal has a multi-dot configuration.

The laser source can be any source suitable for laser welding, including carbon dioxide and copper vapour laser sources. Typically the

maximum average power is from 10W to 200W, preferably from 25W to 100W and the maximum peak power is from 10kW to 1kW , preferably from 5kW to 3kW.

In one aspect, the laser energy is appliable in continuous fashion.

In another aspect, the laser energy is appliable is pulsed fashion. Preferably, the laser source has a pulse width of from 0.5 to 20 microseconds and a maximum pulse energy of from 10 to 100 Joules.

Preferably, the seal has a seal width of from 1 to 10mm, more preferably from 2 to 5mm.

Suitably, the base sheet and cover sheet comprise material selected from the group consisting of metal foil, plastic material and paper. Suitable metal foils include aluminium foil having a thickness of from 5 to 100μm, preferably from 10 to 50μm. Suitable plastic materials include polyethylene, polypropylene, polyvinyl chloride and polyethylene terephthalate.

The base sheet and the cover sheet may in one aspect comprise laminates of any suitable materials. The particular laminate structures are chosen to optimise the performance of the blister pack.

Preferably, the base sheet and cover sheet comprise different materials.

Suitably, the method additionally comprises applying laser energy to form score lines on the or each cover sheet or base sheet. The presence of the score lines assists in the opening of the blister pack by a user.

Suitably, the method of the invention is controllable by a computer.

According to another aspect of the present invention there is provided a blister pack formable by the method described above.

Further characteristics of the present invention will become apparent from the following description and accompanying drawings, wherein:

Figure 1 shows a method of forming a blister pack having a single blister in accord with the present invention;

Figure 2 shows a second method of forming a blister pack having a single blister in accord with the present invention;

Figures 3a and 3b show a method of forming a blister pack in the form of an elongate strip in accord with the present invention;

Figures 4a to 4c show blister seal arrangements achievable with the method of the present invention; and

Figure 5 shows a method of forming a blister pack having a single blister from a laminated cover and base sheet in accord with the present invention;

Figure 1 shows an ilustrative method herein. Base sheet 10 has a blister 12 pre-formed therein. Cover sheet 20 is placed on top of the base sheet 10 such that the blister pocket 12 is covered. Laser source 30 directs a laser beam 32 at weld position 40. The laser source 30 is rotated such that a weld is formed between the cover sheet 20 and the periphery of the blister pocket 12.

Figure 2 shows a variation of the method of Figure 1 in which the base sheet 110 and cover sheet 120 are arranged as in Figure 1. The laser source 130 is, however, arranged to direct a laser beam 132 at movable mirror 150. The laser beam 132 is thence, directed towards the weld position 140. In the course of the welding process, the mirror 140 is moved such as to direct the laser beam 132 to form a weld between the cover sheet 120 and the periphery of the blister pocket 112.

Figures 3a and 3b illustrate sequential welding steps in a step-wise process for the formation of a blister pack having a plurality of blisters. Base sheet 210 has a plurality of blisters 212a-d therein. Cover sheet 220 is placed on top of the base sheet 210 such that each of the blister pockets 212a-d is covered. At a welding station, laser source 230 directs a laser beam 232 at weld position 240. In course of the process the base sheet 210 and cover sheet 220 are transported such that each blister 212a-d in turn is brought to the welding station. In forming each weld, the laser source 230 is rotated to direct the laser beam 232 to form a weld between the cover sheet 220 and the periphery of the blister pocket 212a-d.

Figures 4a to 4c show different weld configurations of blister packs formed in accord with the present invention. In each case a top view of the welded cover sheet 320 is shown. In Figure 4a, the welding is a simple line weld 340 of a circular shape (i.e. around the periphery of the pocket of the base sheet below). Score lines 360 have also been laser scored to part of the cover sheet 340 to assist with the opening of the pack. In Figure 4b, a zig-zag weld 340 configuration is shown and in Figure 4c a multi-dot weld 340 configuration is shown. The use of such zig-zags or multi-dots makes the seal formed by the weld 340 easier to break and thus, also improves the openability of the pack.

Figure 5 shows a variation of the method of Figure 1 wherein the blister pack is formed from laminated sheets. The base sheet has a first outer layer 410 comprised of plastic material and a second inner layer 411 comprised of aluminium foil. The base sheet has a blister 412 pre-formed therein. The cover sheet is also comprised of a first outer layer 420 comprised of plastic material and a second inner layer 421 comprised of aluminium foil. The cover sheet is placed on top of the base sheet such that the two aluminium layers 411, 421 contact each other and the blister pocket 412 is covered. Laser source 430 directs a laser beam 432 at weld position 440. The energy of the laser source 430 is tuned such that it will pass through the cover sheet layer of plastic material 420 but weld the two aluminium foil layers 411, 421

together. As in Figure 1 the laser source 430 is rotatable such that a seal may be formed for the entire pocket 412.

The blister pack herein is suitable for containing medicament, particularly for the treatment of respiratory disorders. Appropriate medicaments may thus be selected from, for example, analgesics, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate, ketotifen or nedocromil; antiinfectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti- inflammatories, e.g., beclomethasone dipropionate, fluticasone propionate, flunisolide, budesonide, rofleponide, mometasone furoate or triamcinolone acetonide; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol, terbutaline, isoetharine, tulobuterol, or (-)-4-amino-3,5-dichloro-α-[[[6-[2-(2-pyridinyl)ethoxy] hexyl]methyl] benzenemethanol; diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium, tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or glucagon. It will be clear to a person skilled in the art that, where appropriate, the medicaments may be used in the form of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters (e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or stability of the medicament.

Preferred medicaments are selected from albuterol, salmeterol, fluticasone propionate and beclometasone dipropionate and salts or solvates thereof, e.g., the sulphate of albuterol and the xinafoate of salmeterol.

Medicaments can also be delivered in combinations. Preferred formulations containing combinations of active ingredients contain salbutamol (e.g., as the free base or the sulphate salt) or salmeterol (e.g., as the xinafoate salt) in combination with an antiinflammatory steroid such as a beclomethasone ester (e.g., the dipropionate) or a fluticasone ester (e.g., the propionate).

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims and may include, by way of example and without limitation, one or more of the following claims:

CLAIMS

1. A method of forming a blister pack comprising contacting a base sheet having a blister pocket therein with a cover sheet and applying laser energy to form a seal between said cover sheet and said blister pocket of said base sheet.

2. A method according to claim 1, wherein the base sheet has a plurality of blister pockets therein and laser energy is applied to form a seal between the cover sheet and each blister pocket of said base sheet.

3. A method according to claim 2, wherein the base sheet and cover sheet are elongate and the base sheet has a plurality of blister pockets spaced therealong.

4. A method according to claim 3, wherein laser energy is applied to seal each blister pocket of the elongate base sheet in a sequential fashion.

5. A method according to any of claims 1 to 4 additionally comprising pre-filling the or each blister pocket with medicament.

6. A method according to claim 5, wherein the medicament is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof.

7. A method according to either of claims 5 or 6, wherein the medicament is in dry powder form.

8. A method according to any of claims 1 to 7, wherein the laser energy derives from a laser source which is movable relative to the base and cover sheet to enable correct positioning of the seal.

9. A method according to any of claims 1 to 7, wherein the laser energy derives from a fixed laser source and the base and cover sheet are movable to enable correct positioning of the seal.

10. A method according to any of claims 1 to 7, wherein the laser energy is guidable by means of a guide mechanism to enable correct positioning of the seal.

11. A method according to claim 10, wherein said guide mechanism includes one or more movable mirrors.

12. A method according to any of claims 1 to 11, wherein the seal is a hermetic seal.

13. A method according to any of claims 1 to 12, wherein the seal has a zig-zag configuration.

14. A method according to any of claims 1 to 12, wherein the seal has a multi-dot configuration.

15. A method according to any of claims 1 to 14, wherein the laser energy is supplied by a laser source having a maximum average power of from 10W to 200W, and a maximum peak power of from 1kW to 10kW.

16. A method according to any of claims 1 to 15, wherein the laser energy is appliable in continuous fashion.

17. A method according to any of claims 1 to 15, wherein the laser energy is appliable is pulsed fashion.

18. A method according to claim 17, wherein the laser source has a pulse width of from 0.5 to 20 microseconds and a maximum pulse energy of from 10 to 100 Joules.

19. A method according to any of claims 1 to 18, wherein the seal has a seal width of from 1 to 10mm, more preferably from 2 to 5mm.

20. A method according to any of claims 1 to 19, wherein, the base sheet and cover sheet comprise material selected from the group consisting of metal foil, plastic material and paper.

21. A method according to claim 20, wherein the base sheet and cover sheet comprise different materials.

22. A method according to either of claims 20 or 21, wherein the base sheet and/or the cover sheet comprises a laminate.

23. A method according to any of claims 1 to 22, additionally comprising applying laser energy to form score lines on the or each cover sheet or base sheet.

24. A method according to any of claims 1 to 23, wherein the method is controllable by a computer.

25. Blister pack formable by the method of any of claims 1 to 24.

ABSTRACT

There is provided a method of forming a blister pack comprising contacting a base sheet having a blister pocket therein with a cover sheet and applying laser energy to form a seal between said cover sheet and said blister pocket of said base sheet. The blister pack is preferably in the form of an elongate strip. The blister pack is suitable for the containment of medicament in dry powder form.

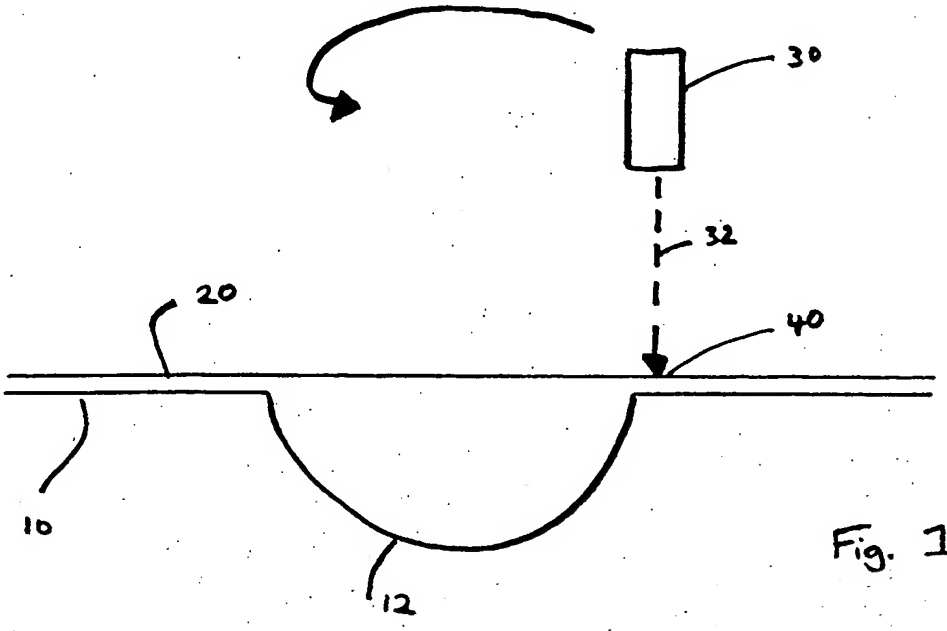

Fig. 1

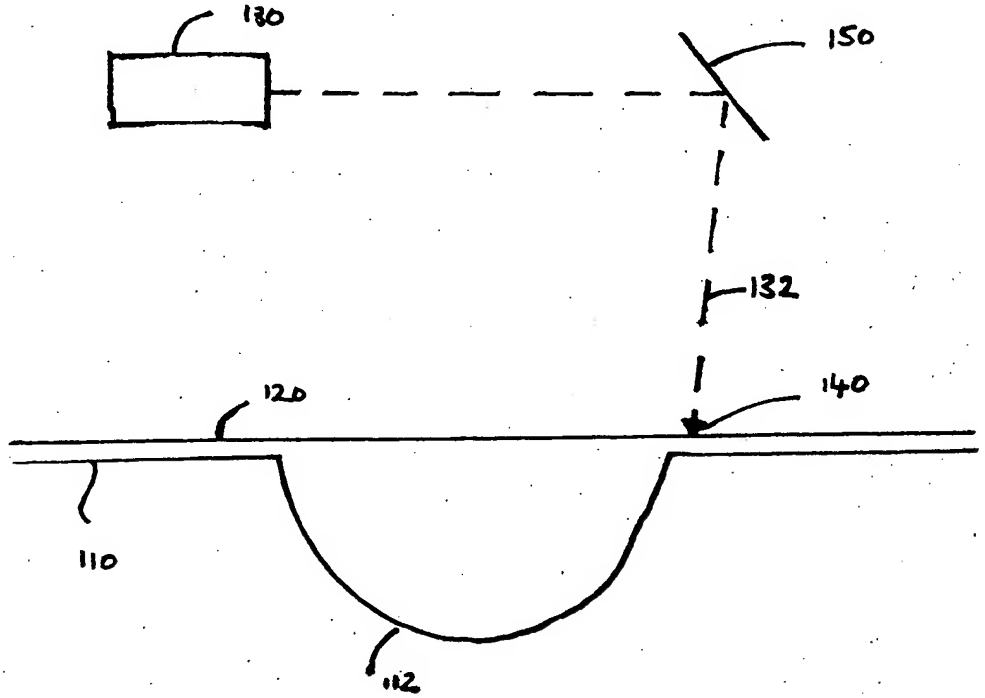

Fig. 2

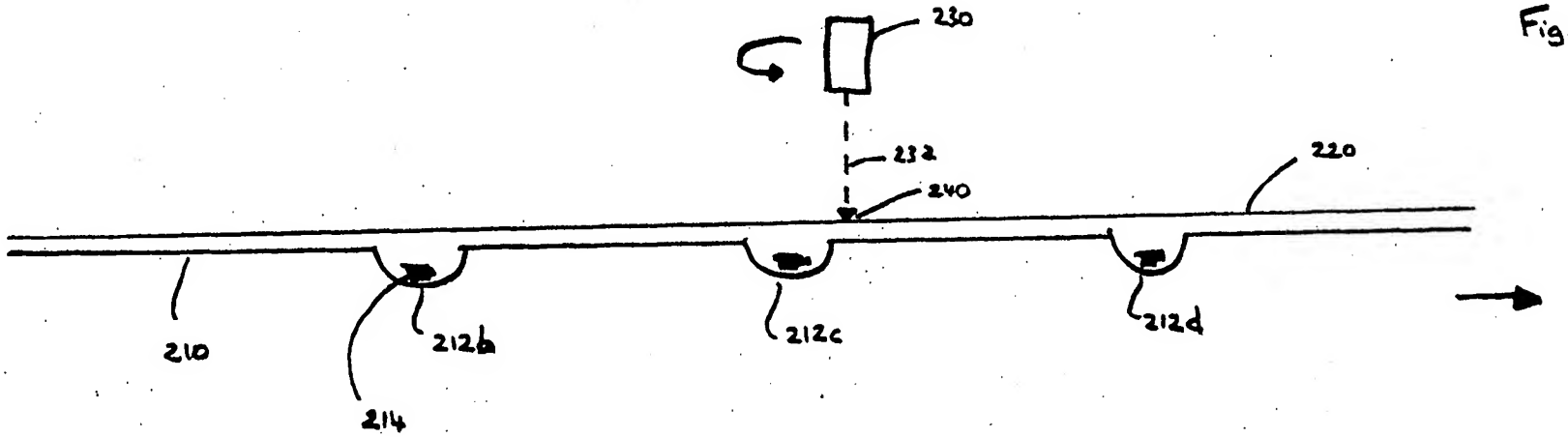
230
232
240
220
210
214
212b
212c
212d

Fig. 3a

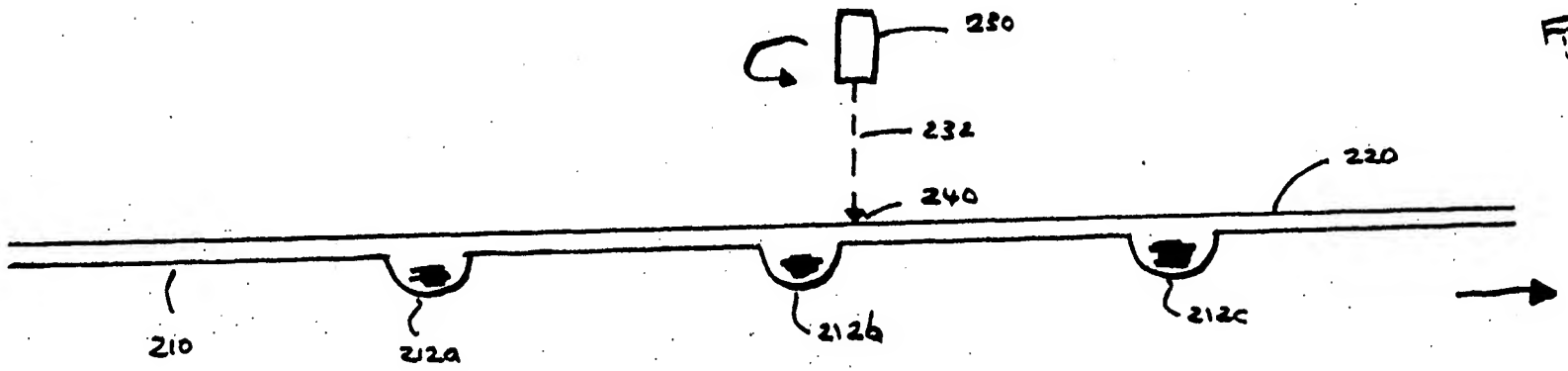
250
232
240
220
210
212a
212b
212c

Fig. 3b

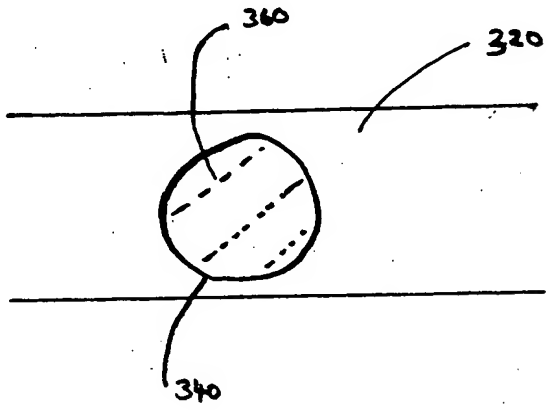

Fig. 4a

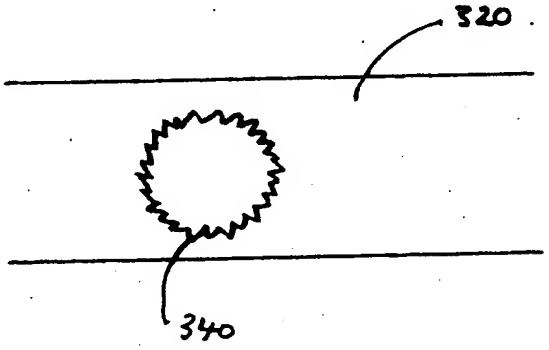

Fig. 4b

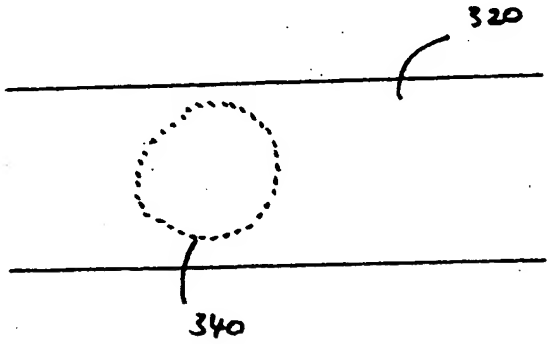

Fig. 4c

Fig. 5